DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Bethesda MD 20892

May 5, 1992

Our Reference Nos: 88-0659, 88-0660

Bernardita Mendez, Ph.D.
Chiron Corporation
4560 Horton Street
Emeryville, CA 94608

Dear Dr. Mendez:

Enclosed is a product license which authorizes Chiron Corporation, U.S. License No. 1106, to manufacture and ship for sale, barter, or exchange in interstate and foreign commerce Aldesleukin.

Aldesleukin is indicated for the treatment of adults (≥ 18 years old) with metastatic renal cell carcinoma. In accordance with approved labeling, your product will bear the tradename Proleukin®, and will be marketed in 22 million (1.3 mg) IU fill size single-use vials for intravenous use. The product will be manufactured at the 1400 Fifty-Third Street location. We note that Cetus Oncology Corporation, Emeryville, California, a corporate subsidiary of Chiron will be the distributor for Aldesleukin.

You are requested to submit samples of each future lot of the product together with protocols showing results of all applicable tests. No lots of product shall be distributed until notification of release is received from the Director, Center for Biologics Evaluation and Research.

The dating period for this product shall be 18 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated product. Results of ongoing stability studies should be submitted at regular intervals throughout the dating period as they become available.

Accordingly, the amendment to your establishment license application to include facilities leased from Cetus Corporation, 1400 Fifty-Third Street, Emeryville, California has been accepted. Therefore Establishment License No. 1106 is hereby reissued to Chiron Corporation with designations of two locations in Emeryville, California, effective this date.

Any changes in the manufacture, packaging or labeling of the product or in the manufacturing facilities will require the submission of an amendment to either your product or establishment license application for our review and written approval prior to implementation.

We acknowledge the written commitments specified in your letter of May 1, 1992, including the following:

1. To conduct additional studies into the effects of SDS on the pharmacology of Aldesleukin;

2. To conduct additional studies on the effects of the use of albumin in the diluent for Aldesleukin;

3. To obtain additional clinical data to: 1) determine the effects of antibodies and elevated creatinine on the pharmacokinetics of Aldesleukin; 2) obtain further data to identify the duration of tumor response; and 3) determine factors predictive of response to Aldesleukin therapy;

4. To conduct ongoing stability studies as specified and to withdraw from the market any lot which fails to meet product specifications.

Furthermore, as noted in your letter of February 10, 1992, it is our understanding that no Aldesleukin product manufactured in the renovated Process Development Unit (PDU) facility can be distributed for commercial use prior to submission and approval of an Establishment License Application amendment which covers the PDU changes.

You are requested to submit adverse experience reports in accordance with the requirements for postmarketing reporting of adverse drug experiences (21 CFR 314.80) until such time that specific reporting requirements for biological products become effective. All experience reports should be prominently labeled as "BIOLOGICAL PRODUCT" and be submitted to the Division of Biostatistics and Epidemiology, HFB-250, Attn: Adverse Experience Reporting, Center for Biologics Evaluation and Research, Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892.

Please submit three copies of final printed labeling at the time of use and include part II of the label transmittal form with completed implementation information. In addition, advertising and promotional labeling should be submitted for review and approval prior to the initial publication of any advertisement and prior to the initial dissemination of any promotional labeling.

All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

Please acknowledge receipt of the enclosed licenses to the Director, Division of Product Certification, HFB-240, Center for Biologics Evaluation and Research.

Sincerely yours,

Kathryn C. Zoon, Ph.D.
Director
Center for Biologics
Evaluation and Research

Enclosures